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RESEARCH ARTICLE

Mortality of myasthenia gravis: a national population-based study in China

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Abstract

Objective: As a potentially life-threatening condition, myasthenia gravis (MG) has limited epidemiological studies on mortality. We aim to provide demographic distribution, geographical variation, and temporal trend of MG-related mortality in China. **Methods**: The national population-based analysis was conducted based on records derived from the National Mortality Surveillance System of China. All deaths related to MG were identified from 2013 to 2020, and MG-related mortality was evaluated by sex, age, location, and year. **Results**: A total of 4224 deaths were related to MG during 2013–2020, and the median age at death of MG was 59.45 years, significantly lower than that in the general population (75.47 years, $P < 0.05$). In 2020, the age-standardized mortality rate of MG was 1.86 per million people and markedly higher in males than in females (2.37 vs. 1.31 per million). The mortality rate per million was lower than 1 in young children, peaking at 2.83 only in males (vs. 0.36 in females) aged 10–19 years, and substantially increased with age, reaching the highest rate of 13.31 for males and 10.58 for females aged 80 years and older. Geographical disparity across China was observed with the highest age-standardized mortality rate in Southwest (2.53 per million). From 2013 to 2020, MG-related mortality rate showed an increasing trend with the average annual percentage change of 3.5% (95% CI, 1.4–5.6). The notable increases occurred in age 10–19 years and over 70 years. **Interpretation**: In China, MG-related mortality was notably high among adolescent males and the elderly. The increasing death burden due to MG highlight challenges to disease management.

Introduction

Myasthenia gravis (MG) is an autoimmune neuromuscular junction disorder, caused by autoantibodies attacking postsynaptic components and impairing neuromuscular transmission. Skeletal muscle weakness and fatigability are the most common clinical manifestations of MG, and myasthenic crisis with respiratory muscles involvement is a life-threatening condition that requires mechanical ventilation and intensive care for patients with MG.[1] MG can strike at any age with fluctuating symptoms and usually lead to moderate to severe impairment of health-related quality of life.[2] Previous epidemiological studies mainly described the incidence and prevalence of MG which varied from around 10 to 30 per million and 100 to 350 per million people, respectively, and demonstrated a rising trend in MG morbidity globally, particularly among older people.[1,3,4] However, few national population-based studies were conducted to report the mortality of MG.

Some register-based epidemiological studies undertaken in European and American countries indicated that MG with modern treatment has favorable prognosis, regarding long-term survival for decades and a similar mortality rate to that of the general population.[5–7] However, other

research suggested that patients with MG had a higher mortality rate and shorter survival than the matched general population.[8,9] Additional investigations based on multicenter or monocenter cohorts mainly determined hospital mortality of MG or myasthenic crisis, which has substantially decreased from more than 50% to 2.2%–22.0% as a result of immune intervention and intensive care management improvements.[10–12] Meanwhile, instead of respiratory disease associated with myasthenia crisis, comorbidities such as cardiovascular disease and cancer were shown to be the main underlying cause of death in patients with MG.[5,7,13]

However, as the most populous country in the world, mortality study on MG in China was scarce and limited to hospital inpatients or single-hospital survey with variable hospital mortality rate of 1.47–18.6%.[14–16] With the rapid aging population and rising MG morbidity among the elderly, it is essential to assess the mortality pattern of patients with MG to enhance therapeutic management and clinical outcomes.

Therefore, this study was performed to investigate the demographic distribution, geographical variation, and temporal trend of MG-related mortality in China from 2013 to 2020, utilizing nationally representative data from the National Mortality Surveillance System.

Methods

Ethics approval

This study was approved by the ethics committee of Xuanwu Hospital, Capital Medical University, China (No. 2022100). The secondary analysis was performed by using the de-identified data, and informed consent was not required.

Data source

This study was a nationwide population-based retrospective analysis in China. The mortality data were obtained from the National Mortality Surveillance System (NMSS),[17] which covers a population of 323.8 million people (24.3% of the total population of China) with 605 disease surveillance points (DSPs) across 31 provinces in China. The DSPs system was first established in 1978, and has been continuously improved and expanded in the whole country. In 2013, China's National Health and Family Planning Commission combined the DSPs system with the vital registration system to create the new NMSS, which provides reliable and comprehensive information on mortality and cause of death in the country. Based on multistage cluster sampling and the extensive population coverage, the NMSS data are nationally and provincially representative of the entire population in mainland China, and have been widely used for healthy policy development and disease burden assessment in China and worldwide.[18–20] Data quality was detailed in previous studies, and the mortality rates were adjusted by underreporting rates.[21–23] All deaths related to this study were extracted for the period from 2013 to 2020.

Study population

The death related to myasthenia gravis was defined by the diagnosis of MG as either the underlying cause of death or contributing cause of death, recorded on the standard death certificate.[24,25] All MG-related deaths were identified with the specific code of G70.0 according to the International statistical classification of diseases, 10th revision (ICD-10). The basic information was collected from death certificates, including age at death, sex, education level, place of death, and healthcare institutions that determined the cause of death.

The causes of death with the exception of MG listed on the death certificates were grouped into several key categories, including respiratory disease, cardiac disease, cerebrovascular disease, other neurological disease, cancer (thymoma and other cancers), diabetes, and autoimmune disease.

Statistical analysis

The crude mortality rate (CMR) was calculated by year, age, sex, and location. For age-specific mortality, the population were divided into nine age groups with 0–9 years, 10–19 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, 70–79 years, and 80 years and older. The age-standardized mortality rate was calculated using the direct standardization method based on the reference population from the sixth population census of China carried out in 2010.[26]

The temporal trends of MG-related mortality from 2013 to 2020 were examined by the average annual percentage change (AAPC). The AAPC of the age-standardized mortality rate was estimated using joinpoint regression models performed with Joinpoint Regression Program (version 4.8.0.1, National Cancer Institute), and is considered significant when its value is different from zero at the alpha of 0.05.[27–29] The geographic distribution of MG-related mortality was described in seven major geographical regions across China, including Northeast, North China, Northwest, East China, Central China, Southwest, and South China.[30] For visualization, a vector map was constructed using a geographic information system (ArcGIS version 10.7 software).

Continuous variables were presented as mean ± standard deviation (SD) or median with interquartile rang (IQR); categorical variables were presented as absolute

values with percentages. The Mann–Whitney U-test was used for comparison of data with a non-parametric distribution. The chi-squared test was used for comparison of the mortality rate among different regions. A two-sided $P < 0.05$ was considered statistically significant. All statistical analysis was conducted using SAS version 9.4 and R version 4.1.2.

Results

Characteristics of MG-related deaths in China

During the study period of 2013 to 2020, there were 4224 deaths related to myasthenia gravis in the 605 DSPs of the NMSS across China, 2501 (59.21%) of whom were men (Table 1). The decedents with MG had median age of 59.45 years (interquartile range [IQR], 44.09 to 71.36), which was significantly lower than the general population (75.47 years, IQR 63.62 to 83.66; $P < 0.05$). Male decedents died at a median age of 56.02 years (IQR 32.86 to 68.20), significantly younger than females (63.81 years, IQR 51.23 to 75.77; $P < 0.05$). According to death certificates, 26.42% of MG deaths occurred in healthcare institutions, and 67.47% of those deaths occurred at home. Approximately 97.14% of MG-related deaths were determined by healthcare institutions, with tertiary hospitals accounting for 67.26%.

Among all deaths related to MG during the study period, MG remained to be the predominant underlying cause of death, accounting for 87.19%. Other underlying causes of death were consecutively cancer (3.24%), other neurological disease (2.06%), ischemic heart diseases (1.68%), respiratory infection (1.09%), and cerebrovascular disease (1.02%) (Fig. 1A). Meanwhile, when MG was identified as the underlying cause of death, the leading contributing cause was respiratory disease (32.26%), followed by cardiac disease (10.07%) (Fig. 1B).

MG-related mortality rate in 2020

In 2020, among all deaths reported from the NMSS, 0.30‰ were identified as MG-related deaths, corresponding to the crude MG-related mortality rate of 2.09 per million people. Accordingly, we acquired the national estimate of 2950 MG-related deaths based on the total population of the 31 provinces of mainland China in line with the 2020 Population Census of China. In addition, the age-standardized mortality rate of MG in 2020 was 1.86 per million people, which was higher in males (2.37 per million people) than in females (1.31 per million people), with the male to female mortality ratio of 1.81 (Table 2).

MG-related mortality differs substantially by age (Fig. 2A and B). Overall, the number of MG-related deaths in different age groups showed a bimodal distribution, with the peak at age 10–19 years and 60–69 years. Nearly one-tenth (9.83%) of MG deaths occurred under the age of 20, while more than three-quarters (77.50%) of MG deaths occurred over the age of 40. For males, the age-specific mortality rate was lower than 1 per million people among children under 10 years old, then strikingly increased to a small peak of 2.83 per million people at the age of 10–19 years, and subsequently declined until the age of 39. After 40 years old, the mortality rate rose sharply by

Table 1. Characteristics of MG-related deaths in the NMSS of China during the study period of 2013 to 2020.

Characteristics	Total	Male	Female
Number, *n* (%)	4224 (100)	2501 (59.21)	1723 (40.79)
Location, *n* (%)			
Urban	1875 (44.39)	1028 (41.10)	847 (49.16)
Rural	2349 (55.61)	1473 (58.90)	876 (50.84)
Age at death (years)			
Mean (SD)	55.88 (21.14)	51.74 (21.96)	61.89 (18.30)
Median (IQR)	59.45 (44.09–71.36)	56.02 (32.86–68.20)	63.81 (51.23–75.77)
Annual average mortality rate (per million)	1.85	2.14	1.54
Educational level, *n* (%)			
Postsecondary and tertiary education	221 (5.23)	151 (6.04)	70 (4.06)
Upper secondary education	552 (13.07)	341 (13.63)	211 (12.25)
Primary and lower secondary education	3415 (80.85)	1990 (79.57)	1425 (82.70)
Unknown	36 (0.85)	19 (0.76)	17 (0.99)
Place of death, *n* (%)			
Healthcare institutions	1116 (26.42)	656 (26.23)	460 (26.70)
Home	2850 (67.47)	1703 (68.09)	1147 (66.57)
Other places	258 (6.11)	142 (5.68)	116 (6.73)
Healthcare institutions determined the causes of deaths, *n* (%)			
Tertiary hospitals	2841 (67.26)	1643 (65.69)	1198 (69.53)
Secondary hospitals	1119 (26.49)	701 (28.03)	418 (24.26)
Primary care institution	143 (3.39)	86 (3.44)	57 (3.31)
Other institutions	121 (2.86)	71 (2.84)	50 (2.90)

IQR, interquartile rang; MG, myasthenia gravis; NMSS, National Mortality Surveillance System.

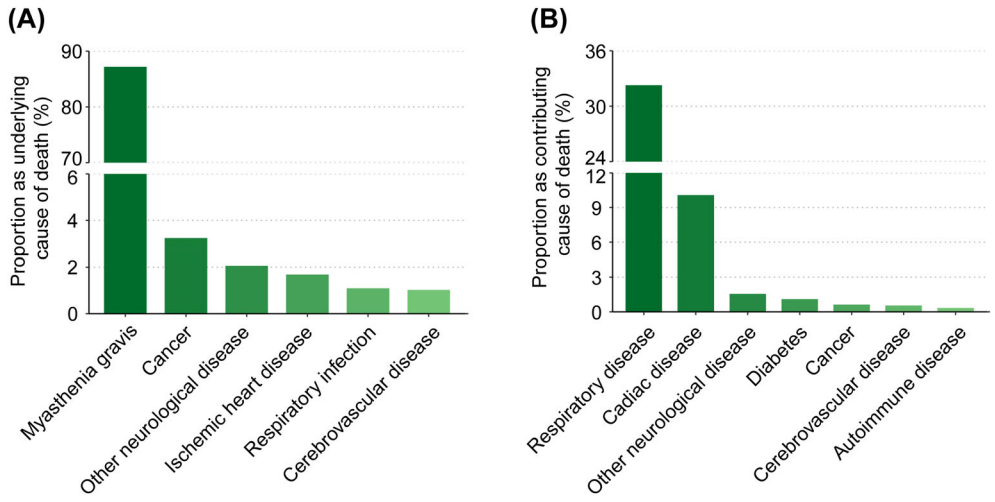

Figure 1. Major underlying and contributing causes of death among decedents with myasthenia gravis in China during 2013–2020. (A) The major underlying causes of death in all death related to myasthenia gravis. (B) The common contributing causes of death in decedents with myasthenia gravis as the underlying cause of death.

Table 2. Crude and age-standardized mortality rate of MG, and temporal trends from 2013 to 2020.

	Crude mortality rate (per million)			Age-standardized mortality rate (per million)			AAPC (95% CI)
	2013	2020	Change (%)	2013	2020	Change (%)	2013–2020
Total	1.55	2.09	34.84	1.51	1.86	23.18	3.5 (1.4–5.6)[a]
Sex							
Male	1.78	2.47	38.76	1.80	2.37	31.67	4.6 (2.8–6.3)[a]
Female	1.31	1.69	29.01	1.22	1.31	7.38	1.5 (−2.4 to 5.5)
Location							
Urban	1.71	2.12	23.98	1.63	1.85	13.50	2.6 (−3.1 to 8.6)
Rural	1.45	2.07	42.76	1.43	1.89	32.17	3.9 (1.7–6.1)[a]
Region							
Southwest	0.97	2.79	187.63	0.94	2.53	169.15	13.9 (5.5–23.0)[a]
North China	1.86	2.17	16.67	1.85	1.90	2.70	1.7 (−2.7 to 6.4)
Central China	1.58	1.99	25.95	1.54	1.90	23.38	5.0 (−0.3 to 10.5)
East China	1.83	2.14	16.94	1.72	1.84	6.98	0.5 (−2.7 to 3.7)
Northeast	2.10	2.39	13.81	1.91	1.78	−6.81	0.9 (−4.4 to 6.5)
South China	1.13	1.49	31.86	1.21	1.48	22.31	5.9 (1.6–10.4)[a]
Northwest	0.97	1.22	25.77	1.04	1.24	19.23	−0.4 (−9.5 to 9.5)

AAPC, Average annual percent change; CI, confidence interval; MG, myasthenia gravis.
[a]Indicates that the AAPC is significantly different from zero at the alpha = 0.05 level.

age, reaching 13.31 per million people in the oldest age group (≥80 years). The mortality rate for females remained below 1 per million until the age of 40 and then steadily increased to 10.58 per million for the oldest age group.

Geographic distribution of MG-related mortality in 2020

At a national level across China, the number of deaths related to MG was higher in rural areas than urban areas with the proportion of 57.69% and 42.31%, respectively, while the crude mortality rate of MG (2.12 per million people in urban area and 2.07 per million people in rural areas) and the age-standardized mortality rate (1.85 per million people in urban area and 1.89 per million people in rural areas) were relatively similar in these two areas (Table 2).

At the subnational level divided into the seven geographical regions of China (Table 2), the crude mortality rate of MG was 2.79 per million people for Southwest,

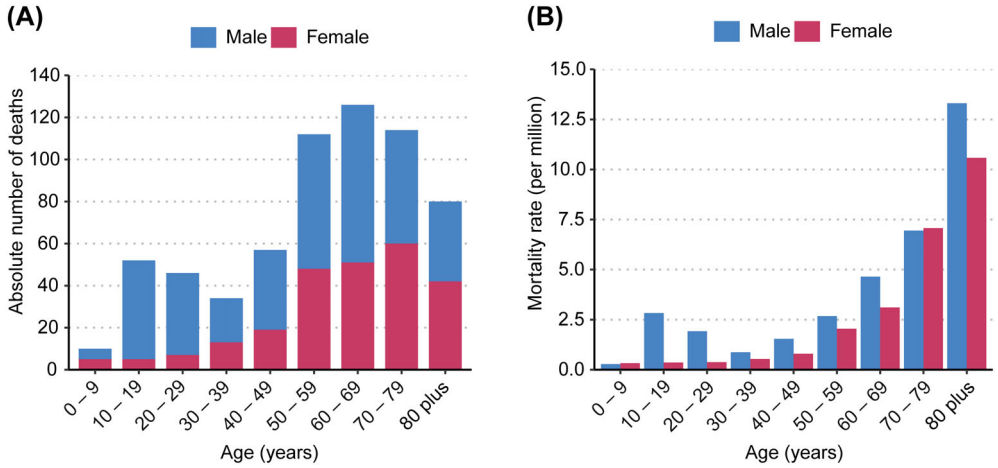

Figure 2. Number of deaths (A) and mortality rate (B) of myasthenia gravis by age and sex in China, 2020.

2.39 per million people for Northeast, 2.17 per million people for North China, 2.14 per million people for East China, 1.99 per million people for Central China, 1.49 per million people for South China, and 1.22 per million people for Northwest, with significant differences among these regions ($P < 0.05$). Correspondingly, the highest age-standardized mortality rate of MG was in Southwest (2.53 per million people), and the lowest mortality rate was in South China (1.48 per million population) and Northwest (1.24 per million population). Other regions had approximate values of age-standardized mortality rate ranging from 1.78 to 1.90 per million people (Fig. 3).

Temporal trend of MG-related mortality from 2013 to 2020

From 2013 to 2020, the number of MG-related deaths increased by 66.49%, corresponding to a 34.84% increase in the crude MG mortality rate (Table 2, and Table S1 in supplementary materials). The age-standardized MG mortality rate increased by 23.18%, from 1.51 per million people in 2013 to 1.86 per million people in 2020, presenting a significant upward trend with the estimation of 3.5% in AAPC (95% CI, 1.4–5.6; $P < 0.05$) (Fig. 4). For males, the age-standardized MG mortality rate increased by 31.67% from 1.80 per million people in 2013 to 2.37 per million people in 2020, with a significant estimation of 4.6% in AAPC (95% CI, 2.8–6.3; $P < 0.05$). While among females, the age-standardized MG mortality rate increased by 7.38% from 1.22 per million people in 2013 to 1.31 per million people in 2020, with no significant change over time (AAPC: 1.5% [95% CI, −2.4 to 5.5]).

Moreover, the increase of MG mortality over time occurred primarily in adolescents and elderly people over the age of 70 (Fig. 5A and B). Between 2013 and 2020, MG mortality rate in adolescents aged 10–19 years increased by 75.26%, from 0.97 to 1.70 per million population; meanwhile, it increased by 88.12% in adults over 80 years, from 6.23 to 11.72 per population. The AAPC of age-specific MG mortality rates were 7.2% (95% CI, 1.5–13.3), 5.9% (95% CI, 2.2–9.8), and 9.0% (95% CI, 3.2–15.1) for the age group of 10–19 years, 70–79 years, and over 80 years, respectively, all of which showed significant upward trends during the study period.

Discussion

MG is a rare and heterogeneous disease, with different classification according to age at onset, antibody status, clinical phenotype, and associated thymic pathology. This heterogeneity complicates epidemiological investigations on this disease. For the first time in China, our study conducted a nationally representative analysis of the mortality associated with MG in terms of the demographic distribution, geographic variation, and temporal trend. With the large size of 4224 MG-related deaths identified from the NMSS during the eight years, we found that the median age at death of MG was 16 years younger than the general population. In 2020, the overall mortality rate of MG was 2.09 per million people, with notable high rates among adolescent males and the elderly, and displayed an increasing trend from 2013 to 2020. Accordingly, the death burden due to MG highlight a pressing need to raise the profile of and improve the management of MG.

Until recently, there was a dearth of epidemiological data regarding MG mortality. The limited evidence showed the crude mortality rate of MG varied from 0.43 to 2.7 per million people over the past three decades.[5,8,31–33] Most of them were registry-based studies

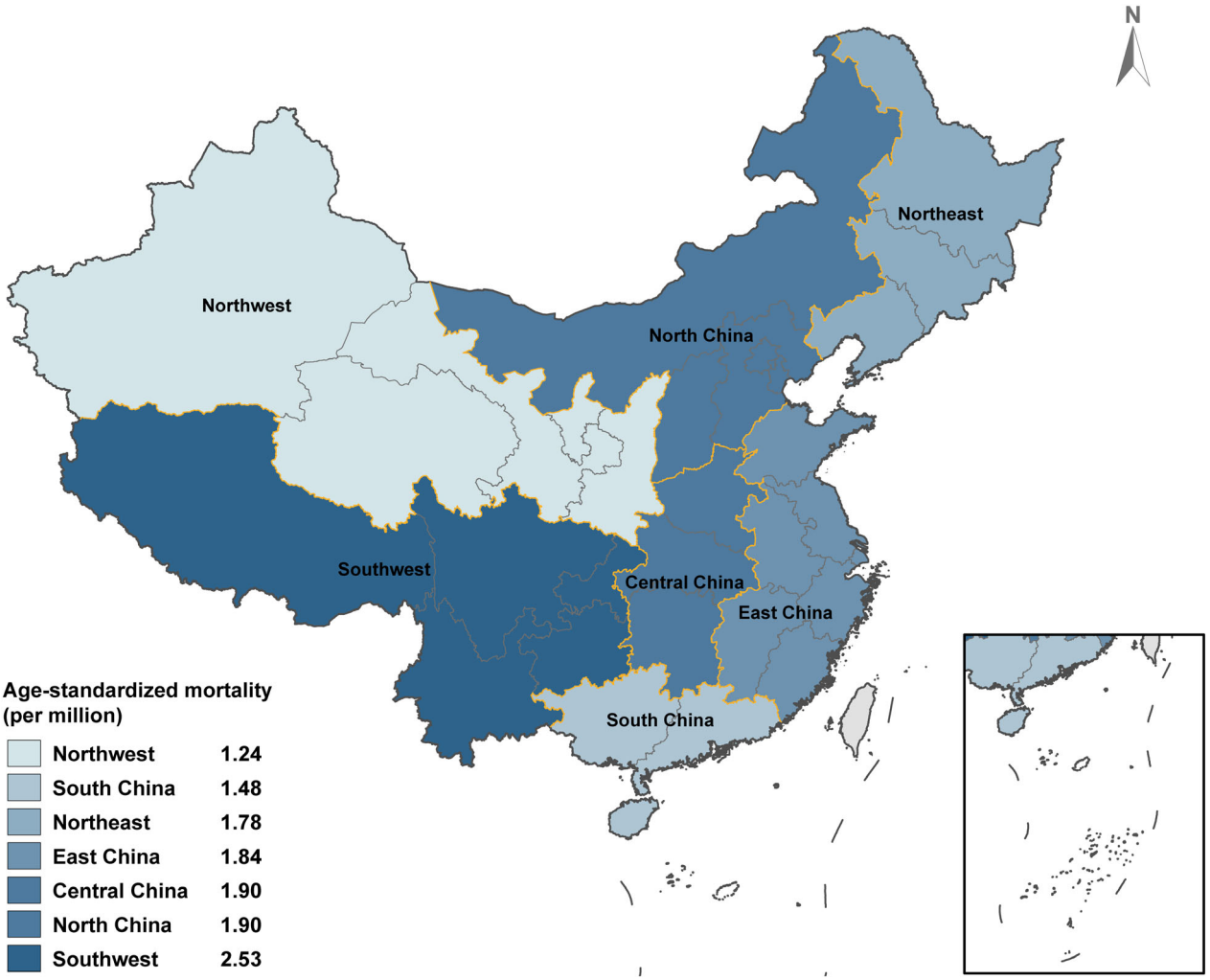

Figure 3. Geographic distribution of the age-standardized mortality rate of myasthenia gravis in China in seven major regions of China in 2020.

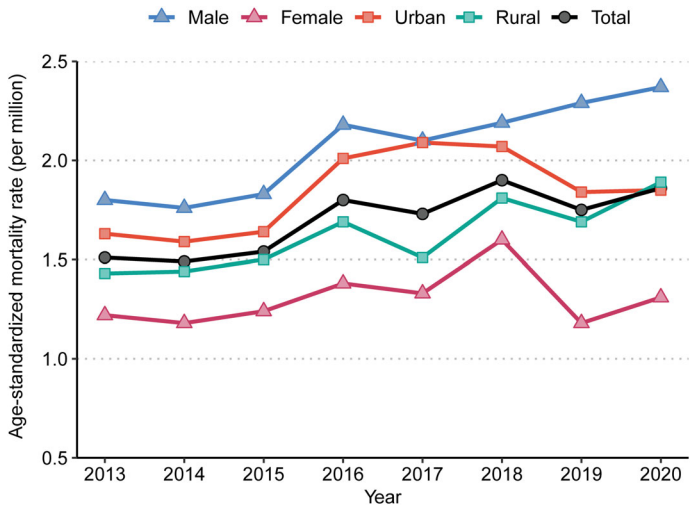

Figure 4. Temporal trend in age-standardized mortality rate of myasthenia gravis by sex and area in China from 2013 to 2020.

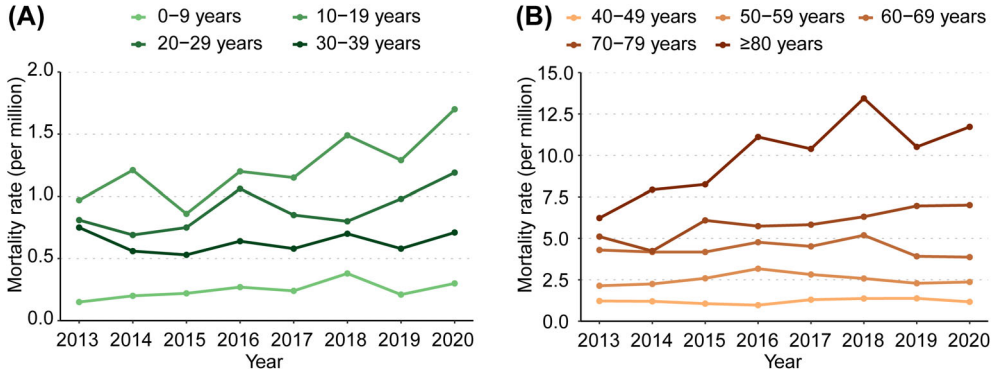

Figure 5. Temporal trend in age-specific mortality rates of myasthenia gravis in China from 2013 to 2020, with (A) for people aged under 40 years and (B) for people aged 40 years and older.

that analyzed medical records in several European countries over a period of around 15–30 years to calculate the annual average mortality rate. Recently, a nationwide cohort study in Poland employing health insurance records estimated the all-cause mortality rate of MG to be 8.1 per million people in 2018.[34] In our study, the mortality data were derived from an integrated national mortality surveillance system, which covers nearly one-quarter of China's population and has been demonstrated to be nationally representative.[17] We initially reported that the overall crude mortality rate of MG in 2020 was 2.09 per million people in China, comparable to other countries. Considering the COVID-19 outbreak in 2020 and its impact on many facets of health, we further observed that none of all MG-related deaths in our study had COVID-19, and the temporal trend did not show abnormal increase around 2020 in MG-related mortality. In fact, a recent study in China reported that during the three months of the COVID-19 outbreak (January 1 to March 31, 2020), excess mortality due to non-COVID-19 related pneumonia in Wuhan city was mainly associated with certain noncommunicable diseases including cardiovascular disease, hypertensive heart disease, and diabetes; meanwhile, no increase in overall mortality was found in other parts of China.[35] Nonetheless, it is worth paying attention to the long-term impact of COVID-19 on patients with MG.

MG mortality in Chinese adults was higher in males than females and rose with age beyond 40 for both sexes, similar with the male bias and age-related rise in MG mortality reported in prior studies from the Danish and Belgrade populations.[5,8] The researchers observed that early-onset MG (≤50 years old) had a low mortality rate with female preponderance, consistent with the notion that female and early-onset age were prognostic factors of favorable survival in patients with MG, and late-onset MG (>50 years old) showed a male predominance, which may partially explain the male bias and rise with age of MG mortality.[36,37] However, a recent research on inpatients in China estimated that the incidence in females was slightly higher than that in males, as well as a higher admission mortality rate in females than in males.[16] Considering that more than 70% of MG death occurred outside of hospitals, our study elaborated a more valid mortality rate representing the nationwide population in mainland China.

It is worth noting that there was a small peak of MG mortality in adolescent males. Juvenile myasthenia gravis (JMG) is a rare subtype of early-onset myasthenia gravis (≤18 years old). According to the current data, JMG was more prevalent in China than in western countries,[38] accounting for around 45% and 5% of MG cases, respectively.[39,40] Although JMG in China was mainly reported to be ocular myasthenia gravis and often had good prognosis, about half of patients exhibited elevated acetylcholine receptor antibodies, which were considered to be associated with increased risk of generalization.[40,41] A long-term follow-up study on JMG with disease onset under 14 years in China revealed that 95% of patients were ocular MG, 18% of which developed into generalized MG, and more than 50% of patients were exacerbated, primarily due to discontinuation of immunotherapy.[42] Similarly, a Norwegian study on the long-term outcome of prepubertal and postpubertal onset JMG,[43] reported that whereas 59% JMG initially presented with ocular symptoms, nearly 50% of patients progressed to generalized MG within two years of onset, and myasthenic crisis was more frequent in the prepubertal onset group. Therefore, more complex factors, such as antibody status, puberty, and sex hormones, may affect the clinical feature and outcome of JMG. We were unable to further interpret the reason for the peak of MG mortality in Chinese young men based on the available evidence, but it merits additional consideration and research into the interactions of

genes and environment with JMG, as well as the therapeutic strategy for adolescents.

As immune intervention and mechanical ventilation improved, deaths caused by myasthenia crisis decreased dramatically, implying that MG mortality might decline as well. However, consistent with several studies,[8,32] our results indicated that MG-related mortality exhibited an upward trend over time, primarily in adolescents and the elderly. The following are some possible explanations for this tendency. Firstly, the advancement of antibody testing and the accessibility of neurological services make the diagnosis of MG more reliable and easier in the last decades.[44] Secondly, the benefits of thymectomy and long-term immunosuppressive therapy are controversial in view of their impact on pediatric growth and increased risk for comorbidity and complications, bringing challenges to the management of younger and elderly patients with MG.[45,46] In addition, the life expectancy in China has increased from 76.1 to 77.6 years during the study period.[47] It is reasonable to speculate that the increase of life expectancy together with population aging might contribute to more elderly patients with MG and subsequently lead to more elderly people dying of MG. Given that late-onset MG was more common than early-onset MG, with male predominance and negative prognosis of more life-threatening events in late-onset MG,[1,5,48–50] the above factors may partly explain the significant increase of MG-related mortality in males. Fortunately, the concept of impending myasthenic crisis and manifest myasthenic crisis was clearly defined in the international consensus guidance for management of myasthenia gravis in 2016, which may improve early recognition and intervention on life-threatening events.[45] However, taking into account medication compliance, health expenses and other socioeconomic factors, China is still confronted with many difficulties in the optimal and long-term management of MG.[16,51]

Furthermore, we identified geographical disparities in MG mortality across China, with the highest in the region of Southwest, the lowest in South China and Northwest. Unlike in Northern Europe where reported the higher prevalence in Netherlands than in Norway among patients of antibody-positive MG with AChR or MuSK,[52] the north–south latitude gradient was not shown in China. The incidence of MG was higher in circum-Bohai Sea Zone located in Northern China,[16] which could not explain the distribution of MG mortality. Various factors, besides age and sex, may have important impact on geographical variations of mortality, including economic capacity, clinical practice, and medical insurance policy. Economic development and healthcare reform result in advanced medical service and increased insurance coverage, which have brought benefits to the equalities in access between rural and urban aeras, and across regions.[53] Utilization of inpatient and outpatient care has increased substantially, and are likely to help more patients getting correct diagnosis and improved treatment.[54,55] A recent study based on hospital and healthcare insurance system record in the cities of South China and Northeast regions, indicated that the southern MG population had higher prevalence and proportion of hospitalization than the northern one, possibly affected by disease awareness and utilization of health insurance.[56] Given that most patients with MG need long-term costly immunosuppressive therapy,[57] medical insurance may be vital for ensuring appropriate and adequate treatment, and improving illness outcome. However, the proportion of out-of-pocket expenses in patients with MG was high and increased progressively, suggesting that the current medical insurance policy is inadequate for MG management.[51]

The current study had several limitations since the data used for our analysis were derived from standard death certificates maintained by the National Mortality Surveillance System. First, individual information on MG subgroups for decedents was not available. Given the great heterogeneity of MG, further investigation in conjunction with more detailed medical history are needed to determine the reason of the peak in MG mortality in Chinese young men. Second, we were unable to obtain information on incidence of MG, which impeded to analyze the survival and identify causative factors for MG. Nevertheless, given the specificity of MG diagnostic criteria, false-positive MG cases are unlikely to be included in the death certificates, exhibiting the reliability of the MG mortality rate in Chinese population. Finally, during the study period, the number of reported MG deaths was quite low in some sparsely populated provinces, such as Tibet, Qinghai, and Hainan. We could not exclude the possibility of underestimation for the rarity of MG and hence depicted the geographic distribution at the regional level rather than provincial level to underscore the affected areas by MG in China.

In conclusion, our study, for the first time in China, provides a comprehensive pattern of MG-related mortality with the demographic distribution, geographic variation, and temporal trends during the 8-year study period. The notably high mortality among adolescent and the elderly reveals a substantial risk of death due to MG and challenges to the disease management. Given rapid aging in China, the increasing trends of mortality over time may exacerbate the disease burden associated with MG, which needs more public attention. Unpacking the disparity between rural and urban areas, and among various regions, may inform healthcare providers and disease control priorities in China. As MG is a chronic neuromuscular junction disorder with fluctuating clinical courses,

expanding large-scale collaborative studies with long-term follow-up will immensely benefit to a complete understanding of the disease's heterogeneity and optimizing health management of MG.

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Author Contributions

CZ, PY, and JWH conceived and designed the study. CZ, FW, ZL, PY, and JWH performed the analyses and interpretation. CZ, FW, ZL, and PY prepared the first draft and figures. XMW, LJW, YWD, MGZ, PY, and JWH revised the manuscript for important intellectual content. JY, YR, QFM, and JJL reviewed the results and provided comments. All authors approved the final version of the manuscript.

Conflict of Interest

The authors have no competing interests to disclose.

Data Availability Statement

All data relevant to the study are included in the article or uploaded as supplemental information. Any additional data that may not be directly available will be shared from the corresponding authors upon reasonable request.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. The death number and age-standardized mortality rate for MG in the NMSS of China from 2013 to 2020.

